

A METHOD FOR METHYLIDENATION AND ETHYLIDENATION OF AN ALLYLIC THIOETHER LEADING TO A 2,3-SIGMA-TROPIC REARRANGEMENT. FAILURE OF THE SIMMONS-SMITH REACTION IN THE PRESENCE OF THIOETHERS

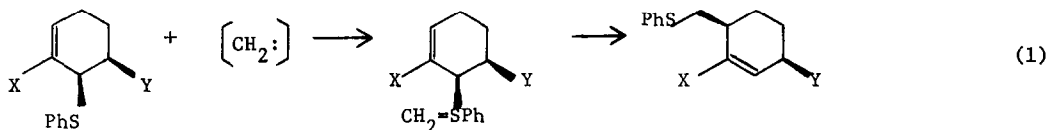
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**Abstract:** Allylic phenylthioethers are converted in one step to homoallylic phenylthioethers by treatment with methylene iodide or ethylidene iodide in the presence of diethylzinc but not zinc-copper or zinc-silver couples; furthermore, Simmons-Smith cyclopropanation of cyclohexene is unsuccessful in the presence of various thioethers.

The  $\text{PhSCH}_2$ - group is particularly versatile in organic synthesis. Raney nickel desulfurization<sup>1</sup> provides a methyl group. Reductive lithiation with lithium naphthalenide<sup>2</sup> yields  $-\text{CH}_2\text{Li}$ . One mole of a chlorinating agent such as N-chlorosuccinimide (NCS) yields the C-chloro derivative<sup>3</sup> which has multiple uses including hydrolysis to an aldehyde<sup>4</sup> and conversion to an  $\alpha$ -(phenylthio)ether for use in the production of  $\alpha$ -lithioethers.<sup>5</sup> The use of two moles of NCS yields the  $-\text{Cl}_2\text{CSPH}$  group which can be hydrolyzed to a thioester or, when a hydrogen atom is present on the adjoining carbon atom, converted to a 1-phenylthio-1-chloroalkene.<sup>6</sup>

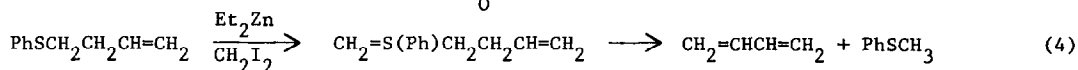
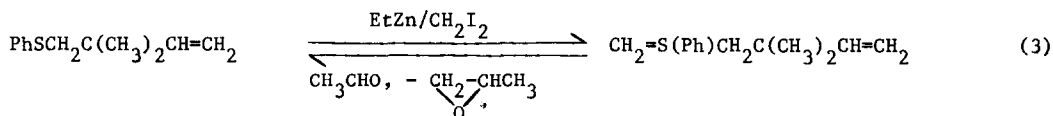
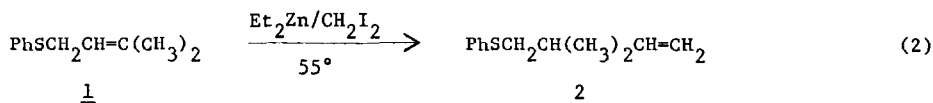
Because Diels-Alder reactions of 2-methoxy-1-phenylthio-1,3-butadienes<sup>7</sup> with dienophiles usually proceed with high or complete stereospecificity<sup>7a,8</sup> a variety of adducts are now readily available with defined stereochemistry. We sought a mild, one-step method of converting the carbon-sulfur chirality of these adducts or their derivatives into carbon-carbon chirality by way of a 2,3-sigmatropic rearrangement of the ylide derived by attack of a carbene on the allylic sulfide (eq.1). Formation of the ylide by deprotonation of the corresponding methyl sulfonium salt would not only involve an extra step but the salt is expected to be quite unstable.<sup>9a</sup>



Although the direct formation of a sulfur ylide by the reaction of a thioether and a carbene has been reported by several groups, all cases involve complex carbenes which are capable of being generated either by strong base-induced  $\alpha$ -elimination in a precursor or by diazoalkane decomposition.<sup>10</sup> Curiously, the Simmons-Smith reaction<sup>11</sup> has never been used to generate an ylide from an allylic thioether despite the known propensity of carbenes or carbenoids to attack divalent sulfur in preference to an olefin.<sup>10b</sup> The reason for this became evident when we found that the combination of an allylic sulfide, methylene iodide, and various zinc-copper and zinc-silver couples<sup>11</sup> or copper powder<sup>12</sup> led only to formation of an insoluble polymer, apparently a poly-methylene. It was shown that the cyclopropanation of cyclohexene under Simmons-Smith conditions was completely suppressed if allyl phenyl sulfide, dimethyl sulfide, or other thioethers were present in the solution; the polymer was again formed, methylene iodide and the sulfide were con-

sumed, and cyclohexene was recovered. That defective reagents or techniques are not responsible for this failure is evident by the demonstration that the same reaction conditions were successful in causing the cyclopropanation of cyclohexene when the sulfide was omitted.

We now report that the desired transformation can be successfully executed by use of a homogeneous solution of diethylzinc<sup>13</sup> and methylene iodide (eq. 2), a combination that has been used previously for the cyclopropanation of an olefin.<sup>14</sup> The poor yields and material balances found in early experiments were avoided by quenching the reaction mixture with acetaldehyde, a procedure which presumably releases the desired homoallylic sulfide from its ylide via epoxide formation (eq. 3).<sup>9b,15</sup>



The yields in a number of cases are recorded in the table.<sup>16</sup> Under the standard reaction conditions, those homoallylic sulfides which can form ylides capable of elimination<sup>10b,17</sup> to dienes are isolated in lower yields; thioanisole is also produced (eq. 4). Fortunately, the use of lower reaction temperatures and longer reaction times led to improved yields. No cyclopropanation products were ever observed. In the case of the optically active ( $[\alpha]_D^{25} = +14^\circ$ ) allylic sulfide derived from *cis*-carveol ( $[\alpha]_D^{25} = -33.4^\circ$ )<sup>18</sup>, the rearrangement product was obtained in optically active ( $[\alpha]_D^{25} = +24^\circ$ ) form (entry 6). As in the Simmons-Smith reaction,<sup>19</sup> the rearrangement was also initiated by ethylidene iodide (entries 8 and 9) but not by 2,2-diiodopropane or 1,1-diiodopentane. Finally, the selenium analogue could also be a substrate (entry 10).

The preparation of 2 (entry 2) should serve as an example of the procedure. Diethylzinc (1.2 ml, 1.4 mmol) was injected into 5 ml of oxygenated,<sup>20</sup> anhydrous benzene at 55°. Sulfide 1 (0.12 g, 0.70 mmol) was injected into the stirring solution. Injection of diiodomethane (0.56 g, 2.1 mmol) caused the reaction solution to become milk-white. The reaction solution usually cleared within the first 2 h of its 24 h at 55°. The heat source was removed and the reaction solution was cooled to ambient temperature prior to the injection of 1 ml of acetaldehyde into the reaction solution.<sup>21</sup> After being stirred for a minimum of 5 min., the quenched reaction solution was poured into a separatory funnel and partitioned between ether and aq.  $\text{NH}_4\text{Cl}$  (buffered to  $\text{pH} \approx 8$ ) solution. The aqueous phase was washed twice with ether. The combined organic phase was dried with  $\text{MgSO}_4$  and concentrated. The residue was diluted with 5% EtOAc in hexanes. The precipitated polymers were removed by employing a silica gel flash-scrub column. The solvent was removed to provide 0.11 g (80%) of 2 which was pure by 300 MHz NMR spectroscopy. Secondary sulfides were found to react more slowly; 48 h was usually allowed.

The application of this procedure to the modification of a Diels-Alder adduct will be reported in a future paper dealing with the synthetic uses of various 1-phenylthio-1,3-butadienes.

Table. Methylidenation and Ethylidenation of Allylic Phenylthioethers and a Phenylselenoether Followed by 2,3-Sigmatropic Rearrangement

Entry	Reactant <sup>a</sup>	Product	(% yield)	Entry	Reactant <sup>a</sup>	Product	(% yield)
1			(55)	6			(78)
2			(80)	7			(72)
3			(79)	8			(70)
4			(76)	9			(71)
5			(75)	10			(75)

<sup>a</sup>The reagent used was  $\text{CH}_2\text{I}_2$ , except where noted. <sup>b</sup>The commercially available alcohol was converted directly into the corresponding sulfide without contamination by the  $\text{SN}2'$  product by use of tributyl phosphine and diphenyl disulfide.<sup>22</sup> <sup>c</sup>I. Fleming, I. Paterson, and A. Pearce, *J. Chem. Soc. P. I.*, 256 (1981). <sup>d</sup>P. M. Atlani, J. F. Biellmann, S. Dube, and J. J. Vicens, *Tetrahedron Lett.*, 2665 (1974); J. Hartman, R. Muthukrishnan, and M. Schlosser, *Helv. Chem. Acta.*, 57, 2261 (1974). <sup>e</sup>A. Itoh, S. Ozawa, K. Oshima, S. Sasaki, H. Yamamoto, T. Hiyama, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 53, 2357 (1980). <sup>f</sup>The reagent used was 1,1-diodoethane.<sup>23</sup> <sup>g</sup>A single product (300 MHz NMR spectroscopy) of unknown stereochemistry. <sup>h</sup>Stereochemistry assigned on basis of assumed mechanism.

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15. Isolation of the presumed epoxide could not be accomplished due to the tendencies of  $\text{Et}_2\text{Zn}$ ,  $\text{EtZnI}$ , or  $\text{ZnI}_2$  to catalyze the polymerization of epoxides.<sup>14c</sup>
16. The structures of all new compounds are consistent with their  $^1\text{H}$  NMR, IR, and mass spectra and with their determined exact masses.
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20. Yields ranged from 0-95% for various runs of the same experiment with deoxygenated benzene whereas an 80% yield was consistently obtained with the oxygen catalyst. Oxygen has been found beneficial in cyclopropanations as well.<sup>14b</sup>
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